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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,122	09/19/2003	Reiner Laus	57636-8127.US01	8703

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EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	
MAIL DATE	**DELIVERY MODE**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,122	LAUS ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,10,12 and 21-30* is/are pending in the application.

4a) Of the above claim(s) *21-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,10 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/22/07 has been entered.

2. Claims 1, 4, 10, 12 and 21-30 are all the pending claims in this application.

3. Claim 1 was amended in the Response of 10/22/07.

4. Claims 21-30 are withdrawn from examination.

5. Claims 1, 4, 10 and 12 are all the pending claims under examination.

Withdrawal of Objections

Information Disclosure Statement

6. Upon closer inspection of the file history, it does not appear that an IDS was filed on January 12, 2004, but that only two IDS' from 12/13/04 and 6/14/06 are of record. The Examiner apologizes for any inconvenience over the original objection.

Applicants' comments on p. 6 of the Response of 10/22/07 are acknowledged.

Specification

7. The objection to the specification for the improper use of trademarks for ISOLEX and AVASTIN is withdrawn in view of Applicants having provided the generic meaning for the trademarks in the amended specification on p. 5 of the Response of 10/22/07.

Applicants' comments on pp. 6-7 of the Response of 10/22/07 and the enclosed Exhibits A (AVASTATIN® datasheet) and B (Baxter ISOLEX® 300i operator manual) are acknowledged.

Withdrawal of Rejections

Claims - 35 USC 103

8. The rejection of Claims 1, 4, 10 and 12 under under 35 U.S.C. 103(a) as being unpatenable over Fikes et al. (US20040037843, published February 26, 2004, filed December 20, 2000) in view Small et al. (J. Clin. Oncol. 18:3894-3903 (December 2000)) as evidenced by Ahmed et al. (J. Pak. Med. Assoc. 52:54-56 (2002)) is withdrawn.

Applicant's arguments filed in the Response of 10/22/07 on p. 14 have been fully considered and are found persuasive. Applicants allege that Fikes only teaches peptides containing epitopes to enhance the immune response against tumor associated antigens such as PAP or GM-CSF. Further amending Claim 1 to recite that the fusion protein comprises the full length hPAP and full length hGM-CSF overcomes the rejection.

Rejections Maintained

Claims - 35 USC §112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

9. The rejection of Claims 1, 4, 10 and 12 under 35 U.S.C. 112, first paragraph, as not being enabled for making or using a immunotherapeutic composition comprising a fusion protein "consisting essentially of" huPAP and huGM-CSF of SEQ ID NOS: 1 and 3, respectively, is maintained.

A. Applicants allege on p. 7 of the Response of 10/22/07 that in amending Claim 1 to recite "consisting essentially of" language "preceding the phrase reciting the characteristics of the fusion protein" and in having deleted the term ""having" in relation to the specific portions of the fusion protein", the immunotherapeutic composition is enabled.

Despite the amendment of Claim 1 to introduce the "consisting essentially of" language in the context of the fusion protein itself rather than the composition as a whole, the claimed composition is not any more enabled than previously recited.

The limitation does not exclude other elements from occurring within the structure of the fusion protein, which materially effect the basic and novel characteristics of the invention, i.e., the fusion protein. In other words, the language does not exclude from the fusion protein the presence of sequences other than those coding for huPAP

and huGM-CSF of SEQ ID NOS: 1 and 3, respectively, and which can otherwise affect the properties of the fusion protein. Additionally, other elements of the fusion protein which may impact or effect the structural or functional properties of the molecule itself can include, *for example*, a signal peptide, a linker peptide, etc. Further, the specification teaches examples of peptide linkers (p. 18, line 34- p. 19, line 6) selected for their ability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides or the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Thus, the instant claim scope in no way excludes the existence of other elements such as a peptide linker, which as taught by the specification, could in fact be selected to interact with the the huPAP and/or huGM-CSF portions of the fusion protein, and thereby materially effect the properties of the protein much less the composition.

The Examiner resubmits that the claimed immunostimulatory composition is not enabled because the claims encompass other elements within the fusion protein that may potentially materially effect the basic and novel characteristics of the composition.

B. In the Office Action of 4/20/07, the Examiner observed an apparent discrepancy between the description for the PAP/GM-CSF fusion protein in the specification (513 amino acids) and for SEQ ID NO:5 (PAP/GM-CSF fusion protein) of the Sequence Listing (144 amino acids). Applicants were specifically requested to address this issue and they have not done so in the Response of 10/22/07.

Applicants' response is incomplete.

Claims - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. The rejection of Claims 1, 4, 10 and 12 under 35 U.S.C. 102(b) as being anticipated by Small et al. (J. Clin. Oncol. 18:3894-3903 (2000); hereinafter referred to as "Small") as evidenced by Ahmed et al. (J. Pak. Med. Assoc. 52:54-56 (2002)) is maintained.

Applicants allege on pp. 7-10 of the Response of 10/22/07 "each preparation of dendritic cells in Small does not necessarily or inevitably result in an immunotherapeutic composition of antigen presenting cells of the instant claims because there is nothing to show that *all patients* in Small had prostate cancer having a moderately to well differentiate cancer grade and a Gleason score of 7 or less." "The mere fact that some patients may have had a prostate cancer with a Gleason score of 7 or less is not sufficient to establish inherency as evidenced by Ahmed since Ahmed "does not address the nature (i.e., Gleason score) of the prostate cancers treated in Small.

Initially, the Examiner points out that none of the instant claims are specifically limited to the composition comprising APC's from a prostate cancer patient with *only* moderate to well differentiated cancer grade and *only* a Gleason score of 7 or less. The claims necessarily encompass APC's from patients of a mixed grade and mixed

Gleason score and some of which based on Small as evidenced by Ahmed could comprise the recited elements of the APC's.

Further, it is not necessary that Ahmed specifically address the exact nature of the prostate cancers treated in Small because Ahmed is cited for showing that one of skill in the art would recognize a patient having a "moderately differentiated" prostate tumors would also be associated with having a Gleason score of 5, 6 or 7 (or 7 or less) (see MPEP 2131.01).

Finally, in amending claim 1 to recite that the fusion protein consists essentially of huPAP (SEQ ID NO:1) and huGM-CSF (SEQ ID NO:3), the fusion protein now has the full length PAP and full length GM-CSF proteins of the Provenge protein of Small. The claimed fusion protein appears to be the same as the prior art Provenge molecule, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

11. The rejection of Claims 1, 4, 10 and 12 under 35 U.S.C. 102(b) as being anticipated by Burch et al. (Clin. Cancer Research 6:2175-2182 (June 2000);

hereinafter referred to as "Burch") as evidenced by Ahmed et al. (J. Pak. Med. Assoc. 52:54-56 (2002)) is maintained.

Applicants have not addressed this outstanding rejection any where in the Response of 10/22/07.

Applicant's response is incomplete.

Claims - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The rejection of Claims 1, 4, 10 and 12 under 35 U.S.C. 103(a) as being unpatenable over Laus et al. (USPN 6,210,662, published April 3, 2001, filed June 24, 1999) in view of Small et al. (J. Clin. Oncol. 18:3894-3903 (December 2000)) as evidenced by Ahmed et al. (J. Pak. Med. Assoc. 52:54-56 (2002)) is maintained.

Applicants allege on pp. 11-14 of the Response of 10/22/07 Laus is a general description for use of protein complexes to stimulate APCs and the present claims are distinguishable in requiring APCs from a particular type of patient, i.e., moderate to well differentiated grade of prostate cancer and a Gleason score of 7 or less. Then

Applicants make contradictory statements within ¶2 on p. 13 of the Response stating in one instance that Small does not provide motivation to select any given cancer population because the patients in Small's clinical trials had "various stages of prostate cancer" then further on they state that "Small is directed to treatment of advanced prostate cancer." Applicants further allege that Ahmed is irrelevant because it does not specifically address the types of patients in Small.

Laus explicitly teaches PAP-GM-CSF fusion polypeptides (having a gly-ser peptide linker) and exposing APCs ex vivo to the polypeptides to induce T-cytotoxic responses against for example prostate cancer. Laus cannot be any more explicit in its disclosure in using immunotherapeutic compositions comprising APCs from prostate cancer patients which are stimulated ex vivo with PAP-GM-CSF fusion proteins. The comments of Small as evidenced by Ahmed are discussed above. Despite Applicants own uncertainty regarding the teachings of Small, it is more than apparent that one skilled in the art based on the combination of references could have drawn a convincing line of reasoning based on the established scientific principles of the references that some advantage or expected beneficial result would have been produced by their combination (MPEP 2144).

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LAB

/Larry R. Helms/
Supervisory Patent Examiner